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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/661,992	09/14/2000	Friedrich Scheiflinger	237.00	8902

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/661,992	SCHEIFLINGER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-16,18,19,23 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-14,16, 18-19, 23 and 25-29* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/2/04, is acknowledged.

2. Claims 1-4, 7-16, 18-19, 23 and 25-29 are pending.

3. The ECACC deposit information, which was made pursuant to the provisions of the Budapest Treaty, in conjunction with Applicant's statement, filed 7/2/04, are sufficient to overcome the previous rejection of the instant claim 15 based upon the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

4. In view of the amendment filed on 7/2/04, only the following rejection is remained.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4, 7-14, 16, 18-19, 23 and 25-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or an antibody fragment against factor IX/factor IXa which increases the procoagulant activity of FIXa in the presence of FVIII inhibitors, wherein the variable region of said antibody derivative comprises amino acids 1-119 and amino acids 135-242 of SEQ ID NO:82, amino acids 1-121 and amino acids 137-249 of SEQ ID NO: 84 or amino acids 1-122 and amino acids 138-249 of SEQ ID NO: 86 and the specific hybridoma in claim 15, does not reasonably provide enablement for any antibody derivative against factor IX/factor IXa which increases the procoagulant activity of FIXa in claim 1 wherein said antibody derivative increases the procoagulant activity of FIXa in the presence of FVIII inhibitors in claims 2, wherein said
3antibody derivative is chimeric antibodies, humanized antibodies, single chain antibodies, bispecific antibodies, diabodies and di-, oligo- or multimers thereof in claim 4, wherein said CDR3 peptide comprises an amino acid sequence of SEQ ID NOs: 5, 105 or 6 in claim 7, wherein the variable region of said antibody derivative comprises amino acids 1-119/1-121/1-122 or amino acids 135-244, 137-249/ 138-249 of SEQ ID NOs: 82, 84 or 86, in claims 8, 10 and 12, a pharmaceutical preparation comprising an antibody derivative and a pharmaceutically acceptable carrier in claim 18, the preparation additionally comprising factor IXaα and/or factor IXaβ in claim 19, a method of obtaining an antibody or antibody derivative which interacts with factor IX/factor IXa and increases the procoagulatnt activity of Factor IXa, comprising the steps of immunizing an immunocompetenet mouse with an antigen selected from group consisting of FIX, FIXaα, FIXaβ or **fragments thereof** in claim 23 or an antibody or antibody derivative against factor IX/IXa having FVIII-cofactor-like activity which exhibits in a FVIII assay after two hours of incubation a ration of background to measured value of at least 3 in claim 28. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the invention commensurate in scope with these claims for the same reason set forth in the previous Office Action mailed 01/02/04.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the antibodies derivatives having SEQ ID NOs: 82, 84 and 86 and the hybridoma that produce the 99090924-99090926 and 99121614-99121620 antibodies, the specification fails to provide guidance as to how to determine the rest of the CDRs which would encompass any CDRs except the CDR3 recited in claim 7. Further the antibody derivative is made against any fragments of FIX, FIXaα or FIXaβ, the specification fails to provide such fragments.

The CDR3 of SEQ ID NO:105 requires 4 different mutations. It is well known in the art that a single amino acid substitution in CDR3 region correlates with low affinity of an antibody (see Panka et al, supra). Thus it is unpredictable if any functional activity will be shared by two antibodies having less than 100% identity over their CDR3 region.

Despite knowledge in the art for producing monoclonal antibodies to specific sequences, the specification fails to provide guidance regarding which fragments (claim 23) result in variants that retain a similar function. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of variants where the expectation of retaining similar function is unpredictable based on the instant disclosure.

Further, at issue is whether or not the claimed composition of claims 18-19 would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success. Further, claim 19 recites the composition further comprising factor IXaα and/or factor IXaβ, however, it is unclear why the antibodies and the antigen are combined in the same composition. Especially, it is known in the art that such combination would neutralize the antibody and/or the antigen.

Applicant's arguments, filed 7/2/04, have been fully considered, but have not been found convincing.

Applicant has not addressed the stated issues and therefore the rejection is maintained.

7. Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
September 2, 2004

Christina Chan

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